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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,114	ALLNUTT ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,30-35 and 37-48* is/are pending in the application.

4a) Of the above claim(s) *41-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27, 30-35, 37-40 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 7, 2008 has been entered.

Claims 27 and 34 have been amended. Claims 27, 30-35, 37-40 and 48 are under examination in this Office Action. Claims 41-47 have been withdrawn.

Claim Rejections - 35 USC § 102

Rejection of claims 27 and 30-32 under 35 U.S.C. 102(e) as being anticipated by Balloul et al. (US Patent 7,354,591 B2) **is withdrawn** in view of Applicant's arguments.

The rejection is withdrawn because Balloul does not expressly disclose transforming yeast, bacterial or algae host organisms as argued by Applicants. Applicant's arguments that Balloul's VLP does not comprise the second exogenous sequence encoding an antigenic protein are not persuasive as discussed below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection of claim 33 under 35 U.S.C. 102(e) as being anticipated by Balloul et al. (US Patent 7,354,591 B2) **is maintained**.

The rejection of claim 33 is maintained because claim 33 is a product by process claim and the process of claims 27 and 30-32 by which the virus-like particle (VLP) is produced is not limiting. The structure of the virus-like particle disclosed by Balloul is the same as the structure of the claimed particle, as discussed below. The process by which the claimed product is made does not confer further structural components to the claimed VLP.

Claim 33 is interpreted as being drawn to a recombinant virus-like particle (VLP) comprising viral coat protein sequences comprising at least one first exogenous sequence encoding a protein or peptide of interest, wherein the protein or peptide is antigenic or allergenic in the target animal. The viral coat protein further comprises at least one second exogenous sequence encoding a tissue-targeting protein sequence having an affinity for a receptor on tissue in a target animal. It is the Examiner's position that the VLP disclosed by Balloul et al. meets all the structural limitations of the presently claimed VLP, as discussed below.

Applicant's arguments have been fully considered however they fail to persuade. Applicant amended the claims to recite that the protein or peptide is antigenic or allergen in the target animal and that the expressed targeting protein has affinity for a receptor on tissue in a target animal. Applicant argues that Balloul does not disclose two exogenous proteins on the surface of the virus capsid. Applicants argue that Balloul discloses just one exogenous sequence that encodes for ligand that binds to an anti-ligand molecule that is localized at the surface of the target cell. Applicants argue that the present invention provides for three separate and distinct

components, the capsid protein with both the antigen protein and the tissue target protein displayed on the surface of the coat protein.

In response to Applicant's arguments, the Examiner respectfully disagrees that Balloul discloses just one exogenous sequence on the surface of the VLP. It is the Examiner's position that Balloul discloses a virus-like particle comprising a viral coat protein encoding the tissue targeting protein that has an affinity for a receptor on tissue in the target cell (see claims 1-14, Example 5, column 4, lines 30-67, column 5 and column 7, lines 30-67) and additionally encoding a second exogenous sequence encoding for an antigenic peptide (see column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34 or see the cited paragraphs from the Balloul's Patent below). Balloul specifically discloses that the coat protein of his VLP encodes a ligand molecule that has an infection specificity for an anti-ligand molecule present on a target cell (see claim 1). Balloul discloses that his VLP also comprises a nucleic acid encoding an antigenic polypeptide that has therapeutic or prophylactic property conferring immunity and inducing humoral or cellular immune responses (see below). Thus Balloul discloses a VLP comprising a coat protein comprising first exogenous antigenic protein or peptide and the second exogenous sequence encoding a tissue-targeting protein having an affinity for a receptor on a tissue in a target animal as required by the present claims. Thus in view of the above the rejection is maintained.

(below: column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34 of Ballou's Patent)

(57) Although it is possible to obtain empty poxviral particle (also called pseudo-poxviral particle) displaying the specific infection property above-described, according to a preferred embodiment, the **poxviral particle of the invention comprises at least a nucleic acid of**

interest, particularly a recombinant nucleic acid including at least one therapeutic gene placed under the control of the elements allowing its expression in eukaryotic target cells.

(61) In a preferred embodiment, the nucleic acid of interest contains at least one sequence of interest encoding a gene product which is a therapeutic molecule (i.e. a therapeutic gene). A "therapeutic molecule" is one which has a pharmacological or protective activity when administered appropriately to a patient, especially patient suffering from a disease or illness condition or who should be protected against this disease or condition. Such a pharmacological or protective activity is one which is expected to be related to a beneficial effect on the course or a symptom of said disease or said condition. When the skilled man selects in the course of the present invention a gene encoding a therapeutic molecule, he generally relates his choice to results previously obtained and can reasonably expect, without undue experiment other than practicing the invention as claimed, to obtain such pharmacological property. According to the invention, the sequence of interest can be homologous or heterologous to the target cells into which it is introduced. Advantageously said sequence of interest encodes all or part of a polypeptide, especially a **therapeutic or prophylactic polypeptide giving a therapeutic or prophylactic property**. A polypeptide is understood to be any translational product of a polynucleotide regardless of size, and whether glycosylated or not, and includes peptides and proteins. Therapeutic polypeptides include as a primary example those polypeptides that can compensate for defective or deficient proteins in an animal or human organism, or those that act through toxic effects to limit or remove harmful cells from the body. **They can also be immunity conferring polypeptides which act as endogenous antigen to provoke a humoral or cellular response, or both.**

(62) Examples of polypeptides encoded by a therapeutic gene include genes coding for a cytokine (alpha, beta or gamma interferon, interleukin, in particular IL-2, IL-6, IL-10 or IL-12, a tumor necrosis factor (TNF), a colony stimulating factor GM-CSF, C-CSF, M-CSF . . .), a immunostimulatory polypeptide (B7.1, B7.2 and the like), a coagulation factor (FVIII, FIX . . .), a growth factor (Transforming Growth Factor TGF, Fibroblast Growth Factor FGF and the like), an enzyme (urease, renin, thrombin, metalloproteinase, nitric oxide synthase NOS, SOD, catalase . . .), an enzyme inhibitor (alphal-antitrypsin, antithrombin III, viral protease inhibitor, plasminogen activator inhibitor PAI-1), the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) protein, insulin, dystrophin, a MHC antigen of class I or II, a polypeptide that can modulate/regulate expression of cellular genes, a polypeptide capable of inhibiting a bacterial, parasitic or viral infection or its development (**antigenic polypeptides, antigenic epitopes**, transdominant variants inhibiting the action of a native protein by competition . . .), an apoptosis inducer or inhibitor (Bax, Bc12, Bc1X . . .), a cytostatic agent (p21, p 16, Rb . . .), an apolipoprotein (ApoAI, ApoAIV, ApoE . . .), an inhibitor of angiogenesis (angiostatin, endostatin . . .), an angiogenic polypeptide (family of Vascular Endothelial Growth Factors VEGF, FGF family, CCN family including CTGF, Cyr61 and Nov), an oxygen radical scaveyer, a polypeptide having an anti-tumor effect, an antibody, a toxin, an immunotoxin and a marker (beta-galactosidase, luciferase . . .) or any other genes of interest that are recognized in the art as being useful for the treatment or prevention of a clinical condition.

New Rejection

Claims 34, 35, 38, 40 and 48 are rejected under 35 U.S.C. 102(e) as being anticipated by Balloul et al. (US Patent 7,354,591 B2).

Balloul discloses therapeutic compositions comprising virus-like particle comprising a viral coat protein encoding the tissue targeting protein that has an affinity for a receptor on tissue in the target cell (see claims 1-14, Example 5, column 4, lines 30-67, column 5 and column 7, lines 30-67) and additionally encoding a second exogenous sequence encoding for an antigenic peptide (see column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34). It is noted that claim 34 requires that the first exogenous sequence encodes for an antigenic or allergenic protein. Balloul specifically discloses that the coat protein of his VLP encodes a ligand molecule that has an infection specificity for an anti-ligand molecule present on a target cell (see claim 1). Balloul discloses that his VLP also comprises a nucleic acid encoding an antigenic polypeptide that has therapeutic or prophylactic property conferring immunity and inducing humoral or cellular immune responses (see column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34). The viral coat protein of Balloul's VLP has been modified to display foreign proteins or peptides (see column 8, lines 55-67 and Example 5). Thus Balloul discloses a genetic construct comprising a nucleic acid encoding a viral coat protein, the first exogenous antigenic protein or peptide and the second exogenous sequence encoding a tissue-targeting protein having an affinity for a receptor on a tissue in a target animal as required by the present claims. This by this disclosure Balloul anticipates the present claims.

Claim Rejections - 35 USC § 103

Rejection of claims 29, 34-40 and 48 under 35 U.S.C. 103(a) as being unpatentable over Balloul et al. (US Patent 7,354,591 B2) in view of Harris et al. (International Immunology, 1997, Vol. 9, p. 273-280 of record on 2/4/2008) **is withdrawn** in view of Applicant's arguments.

New Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 37 and 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balloul et al. (US Patent 7,354,591 B2) as applied to claim 34 and further in view of Harris et al. (International Immunology, 1997, Vol. 9, p. 273-280 of record on 2/4/2008).

Balloul teaches a therapeutic composition comprising a recombinant virus like particle comprising an exogenous ligand that targets tissue antigens and a second exogenous antigenic protein of interest as discussed above. Balloul does not teach the exogenous protein peptide being an allergen or the exogenous sequence inserted into a region truncated to remove sequence unnecessary for VLP self assembly.

Harris teaches virus like particles expressing peptide epitopes of the major house dust mite allergen Der p1 (see the entire document).

It would have been *prima facie* obvious to provide a VLP expressing a protein or peptide that is an allergen. One would have been motivated to express Harris's major house dust mite

allergen Der p1 in the viral coat protein of Balloul's VLP, because Balloul teaches that antigenic epitopes of interest can be expressed in his VLPs (see column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34). One would have been motivated to express Harris's major house dust mite allergen Der p1 in the viral coat protein of Balloul's VLP because Harris teaches that VLPs serve as a strong antigen presentation system known to induce strong cell mediated immune responses and because Harris was able to in vivo prime the Th1 cells with the house dust mite antigens by administering house dust mite antigen expressing VLPs in mice (see Figures 1-4 and Discussion).

One would have been motivated to insert the exogenous sequence into a region truncated to remove sequence unnecessary for VLP self assembly in order to allow the VLP to assemble and to form a functional virus-like particle.

One would have had a reasonable expectation of success to provide VLPs expressing allergenic epitope peptides because the recombinant virus technology used for making such recombinant VLPs has been well established in the art as evidenced by Balloul and Harris.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 27 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balloul et al. (US Patent 7,354,591 B2) in view of Chapman et al. (US Patent 6,232,099 B1).

Balloul teaches a method of producing recombinant virus-like particle comprising providing viral genome, isolating viral coat protein, inserting the exogenous sequence encoding an antigenic peptide of interest into the coat protein, inserting a second exogenous sequence encoding tissue targeting protein that has an affinity for a receptor on tissue in the target cell,

cloning the viral coat protein into a vector and transforming the chicken embryo fibroblast cells (see column 17, lines 17-40, Example 5, column 4, lines 30-67, column 5 and column 7, lines 30-67column 12, lines 41-52, column 13, lines 40-67 and column 14, lines 1-34).

Balloul does not teach transforming yeast, bacterial or algae host organism.

Chapman teaches producing virus-like particles comprising cloning the viral coat protein sequences into a vector and transforming yeast, plant or bacterial host cells (see column 5, lines 15-20 and 37-64 and Examples 1-3).

It would have been *prima facie* obvious to use yeast, algae or bacterial cells to produce recombinant virus-like particles, because yeast, algae and bacterial cells are well known and widely used host cells that can support replication and production of recombinant proteins including recombinant VLPs as taught by Chapman. One would have been motivated to use Chapman's yeast, plant or bacterial cells to produce Balloul's recombinant virus-like particles because Chapman discloses that virus-like particles can be produced in those host cells. One would have had a reasonable expectation of success to use yeast, plant/algae or bacterial cells to produce the recombinant VLPs because those host cell are successfully used to express recombinant proteins as evidenced by Chapman.

Thus the present invention would have been *prima facie* obvious to the skilled artisan at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648